



National Institutes of Health
National Institute of
Environmental Health Sciences
NTP Interagency Center for the Evaluation
of Alternative Toxicological Methods
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January 30, 2009

Dr. Jerry Smrchek
U.S. National Coordinator for the
OECD Test Guidelines Program
U.S. Environmental Protection Agency
Ariel Rios Building, Mail Code 7403M
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Dear Dr. Smrchek:

On behalf of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), we are pleased to provide the enclosed OECD Standard Project Submission Form (SPSF) proposing a new Guidance Document on Using Cytotoxicity Tests to Estimate Starting Doses for Acute Oral Systemic Toxicity Tests (Enclosure). We request that you submit this as a final SPSF to the OECD Secretariat for consideration at the upcoming March 2009 Meeting of the National Coordinators.

The proposed Guidance Document is based on the results of the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) and European Centre for the Validation of Alternative Methods (ECVAM) co-sponsored international, multi-laboratory validation study of two *in vitro* cytotoxicity test methods. ICCVAM subsequently conducted a comprehensive evaluation that included a public international independent scientific peer review of the validation status of the two methods. The report of the peer review panel, the ICCVAM test method evaluation report, the supporting Background Review Document, the recommended test method protocols, and endorsements for U.S. Federal agencies are all available at http://iccvam.niehs.nih.gov/methods/acutetox/inv_nru_announce.htm

ICCVAM concluded that the two *in vitro* cytotoxicity test methods may be used in a weight-of-evidence approach to determine the starting dose for the current acute oral systemic toxicity protocols (i.e., the Up-and-Down Procedure [UDP], the Acute Toxic Class [ATC] method) which are described in OECD test guidelines 423 and 425. For substances correctly estimated to be nontoxic, the *in vitro* methods can reduce the number of animals required for each *in vivo* test by as much as 50% compared to using default starting doses.

As noted in the SPSF, ICCVAM and NICEATM would be glad to organize and host an expert consultation meeting on the proposed document if this is determined necessary after the initial commenting round by OECD member countries.

We believe that expeditious consideration and endorsement of this SPSF and subsequent adoption of the proposed Guidance Document will significantly reduce and refine animal use for acute oral toxicity testing as this is the most commonly conducted product safety test worldwide. Please feel free to contact us at any time if you have questions about the proposed SPSFs. (Dr. Stokes, tel. 1-919-541-7997, email: stokes@niehs.nih.gov; Dr. Wind, tel. 1-301-504-7246, email: mwind@cpsc.gov.)

Sincerely,

William S. Stokes, D.V.M., D.A.C.L.A.M.
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Director, NTP Interagency Center for
the Evaluation of Alternative
Toxicological Methods (NICEATM)
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Marilyn L. Wind, Ph.D.
Chair, Interagency Coordinating
Committee on the Validation of
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Deputy Associate Executive Director
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U.S. Consumer Product Safety
Commission

Enclosures

cc:
ICCVAM
ICCVAM Acute Toxicity Working Group